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(71) Applicant: 3M INNOVATIVE PROPERTIES COMPANY [US/US]; 3M Center, P.O. Box 33427, Saint Paul, MN 55133-3427 (US).

(72) Inventors: COLEMAN, Patrick, L.; P. O. Box 33427, Saint Paul, MN 55133-3427 (US). CROOKS, Stephen, L.; P.O. Box 33427, Saint Paul, MN 55133-3427 (US). LINDSTROM, Kyle, J.; P.O. Box 33427, Saint Paul, MN 55133-3427 (US). MERRILL, Bryon, A.; P.O. Box 33427, Saint Paul, MN 55133-3427 (US). RICE, Michael, J.; P.O. Box 33427, Saint Paul, MN 55133-3427 (US).

(74) Agents: HOWARD, MarySusan et al.; 3M Innovative Properties Company, Office of Intellectual Property Counsel, P.O. Box 33427, Saint Paul, MN 55133-3427 (US).

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(54) Title: AMIDE SUBSTITUTED IMIDAZOQUINOLINES

(57) Abstract: Imidazoquinoline and tetrahydroimidazoquinoline compounds that contain amide functionality at the 1-position are useful as immune response modifiers. The compounds and compositions of the invention can induce the biosynthesis of various cytokines and are useful in the treatment of a variety of conditions including viral diseases and neoplastic diseases.

# Amide Substituted Imidazoquin lines

## Field of the Invention

This invention relates to imidazoquinoline compounds that have an amide containing substituent at the 1-position, and to pharmaceutical compositions containing such compounds. A further aspect of this invention relates to the use of these compounds as immunomodulators, for inducing cytokine biosynthesis in animals, and in the treatment of diseases, including viral and neoplastic diseases.

## Background of the Invention

The first reliable report on the 1*H*-imidazo[4,5-*c*]quinoline ring system, Backman et al., J. Org. Chem. 15, 1278-1284 (1950) describes the synthesis of 1-(6-methoxy-8-quinolinyl)-2-methyl-1*H*-imidazo[4,5-*c*]quinoline for possible use as an antimalarial agent. Subsequently, syntheses of various substituted 1*H*-imidazo[4,5-*c*] quinolines were reported. For example, Jain et al., J. Med. Chem. 11, pp. 87-92 (1968), synthesized the compound 1-[2-(4-piperidyl)ethyl]-1*H*-imidazo[4,5-*c*]quinoline as a possible anticonvulsant and cardiovascular agent. Also, Baranov et al., Chem. Abs. 85, 94362 (1976), have reported several 2-oxoimidazo[4,5-*c*]quinolines, and Berenyi et al., J. Heterocyclic Chem. 18, 1537-1540 (1981), have reported certain 2-oxoimidazo[4,5-c]quinolines.

Certain 1*H*-imidazo[4,5-*c*]quinolin-4-amines and 1- and 2-substituted derivatives thereof were later found to be useful as antiviral agents, bronchodilators and immunomodulators. These are described in, *inter alia*, U.S. Patent Nos. 4,689,338; 4,698,348; 4,929,624; 5,037,986; 5,268,376; 5,346,905; and 5,389,640, all of which are incorporated herein by reference.

There continues to be interest in the imidazoquinoline ring system. For example, EP 894 797 describes imidazoquinoline compounds that bear an amide containing substituent at the 1- position. The active compounds of this series require a terminal amine substituent that may be incorporated into a heterocyclic ring. As another example, WO 00/09506 describes imidazopyridine and imidazoquinoline compounds that may have an amide or urea containing substituent at the 1-position. The compounds described in this publication as having utility contain a 1-substituent wherein the amide or urea

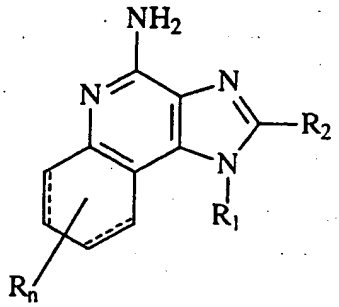
| Cytokine Induction in Human Cells | | |
|---|---|---|
| Example Number | Lowest Effective Concentration (μM) | |
| | Interferon | Tumor Necrosis Factor |
| 155 | 0.01 | 0.1 |
| 156 | 0.001 | 1 |
| 158 | 0.001 | 1 |
| 159 | 0.01 | 1 |
| 172 | 0.0001 | 1 |
| 173 | 0.001 | 1 |
| 174 | 0.001 | 1 |

*Interferon determined using the bioassay method

The present invention has been described with reference to several embodiments thereof. The foregoing detailed description and examples have been provided for clarity of understanding only, and no unnecessary limitations are to be understood therefrom. It will be apparent to those skilled in the art that many changes can be made to the described embodiments without departing from the spirit and scope of the invention. Thus, the scope of the invention should not be limited to the exact details of the compositions and structures described herein, but rather by the language of the claims that follow.

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula (I):



(I)

wherein

$R_1$ is -alkyl-$NR_3$-CO-$R_4$ or -alkenyl-$NR_3$-CO- $R_4$ wherein $R_4$ is aryl, heteroaryl, alkyl or alkenyl, each of which may be unsubstituted or substituted by one or more substituents selected from the group consisting of:

-alkyl;

-alkenyl;

-alkynyl;

-$(alkyl)_{0-1}$-aryl;

-$(alkyl)_{0-1}$-(substituted aryl);

-$(alkyl)_{0-1}$-heteroaryl;

-$(alkyl)_{0-1}$-(substituted heteroaryl);

-O-alkyl;

-O-$(alkyl)_{0-1}$-aryl;

-O-$(alkyl)_{0-1}$-(substituted aryl);

-O-$(alkyl)_{0-1}$-heteroaryl;

-O-$(alkyl)_{0-1}$-(substituted heteroaryl);

-CO-aryl;

-CO-(substituted aryl);

-CO-heteroaryl;

-CO-(substituted heteroaryl);

-COOH;

-CO-O-alkyl;

-CO-alkyl;

-$S(O)_{0-2}$-alkyl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-aryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted aryl);

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-heteroaryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted heteroaryl);

-$P(O)(OR_3)_2$;

-$NR_3$-CO-O-alkyl;

-$N_3$;

-halogen;

-$NO_2$;

-CN;

-haloalkyl;

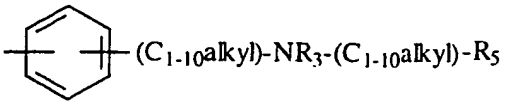
-O-haloalkyl;

-CO-haloalkyl;

-OH;

-SH; and in the case of alkyl, alkenyl, or heterocyclyl, oxo;

or $\mathbf{R_4}$ is




wherein $\mathbf{R_5}$ is an aryl, (substituted aryl), heteroaryl, (substituted heteroaryl), heterocyclyl or (substituted heterocyclyl) group;

$\mathbf{R_2}$ is selected from the group consisting of:

-hydrogen;

-alkyl;

-alkenyl;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-alkyl -O-alkyl;

-alkyl-O-alkenyl; and

-alkyl or alkenyl substituted by one or more substituents selected from the group consisting of:

-OH;

-halogen;

-$N(R_3)_2$;

-$CO\text{-}N(R_3)_2$;

-$CO\text{-}C_{1\text{-}10}$ alkyl;

-$CO\text{-}O\text{-}C_{1\text{-}10}$ alkyl;

-$N_3$;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-CO-aryl; and

-CO-heteroaryl;

each $\mathbf{R_3}$ is independently selected from the group consisting of hydrogen; $C_{1\text{-}10}$ alkyl-heteroaryl; $C_{1\text{-}10}$ alkyl-(substituted heteroaryl); $C_{1\text{-}10}$ alkyl–aryl; $C_{1\text{-}10}$ alkyl–(substituted aryl) and $C_{1\text{-}10}$ alkyl;

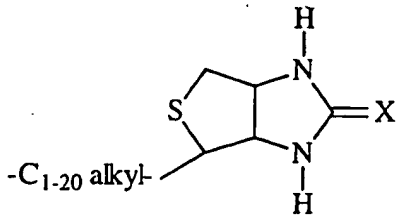
**n** is 0 to 4;

and each **R** present is independently selected from the group consisting of $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halogen and trifluoromethyl, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

2. The composition of claim 1 wherein $R_2$ is hydrogen.

3. The composition of claim 1 wherein $R_2$ is selected from the group consisting of hydrogen; alkyl; alkyl-O-alkyl; $(alkyl)_{0-1}aryl$; and $(alkyl)_{0-1}$ -(substituted aryl).

4. The composition of claim 1 wherein $R_4$ is




wherein X is O, S, or NH.

5. The composition of claim 1 wherein $R_4$ is aryl or heteroaryl that may be unsubstituted or substituted by one or more substituents selected from the group consisting of:

-alkyl;
-alkenyl;
-alkynyl;
$-(alkyl)_{0-1}$-aryl;
$-(alkyl)_{0-1}$-(substituted aryl);
$-(alkyl)_{0-1}$-heteroaryl;
$-(alkyl)_{0-1}$-(substituted heteroaryl);
-O-alkyl;
$-O-(alkyl)_{0-1}$-aryl;
$-O-(alkyl)_{0-1}$-(substituted aryl);
$-O-(alkyl)_{0-1}$-heteroaryl;
$-O-(alkyl)_{0-1}$-(substituted heteroaryl);
-CO-aryl;
-CO-(substituted aryl);
-CO-heteroaryl;
-CO-(substituted heteroaryl);
-COOH;

-CO-O-alkyl;

-CO-alkyl;

-$S(O)_{0-2}$-alkyl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-aryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted aryl);

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-heteroaryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted heteroaryl);

-$NR_3$-CO-O-alkyl;

-$P(O)(OR_3)_2$;

-$N_3$;

-halogen;

-$NO_2$;

-CN;

-haloalkyl;

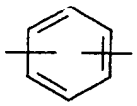
-O-haloalkyl;

-CO-haloalkyl;

-OH; and

-SH.

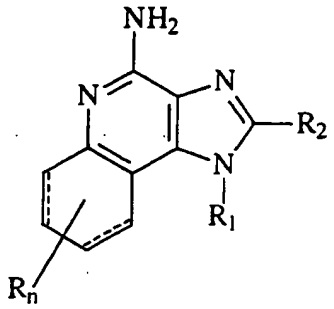
6. The composition of claim 1 wherein $R_4$ is



$(C_{1-10}alkyl)$-$NR_3$-$(C_{1-10}alkyl)$-$R_5$ .

7. The composition of claim 6 wherein $R_5$ is 4-pyridyl.

8. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula (Ia):



(Ia)

wherein

$R_1$ is -alkyl-$NR_3$-CO-$R_4$ or -alkenyl-$NR_3$-CO- $R_4$ wherein $R_4$ is aryl, heteroaryl, alkyl or alkenyl, each of which may be unsubstituted or substituted by one or more substituents selected from the group consisting of:

-heterocyclyl;

-(substituted heterocyclyl);

-$(alkyl)_{0-1}$heterocyclyl;

-$(alkyl)_{0-1}$(substituted heterocyclyl);

-O-$(alkyl)_{0-1}$heterocyclyl;

-O-$(alkyl)_{0-1}$(substituted heterocyclyl);

-$S(O)_{0-2}$–$(alkyl)_{0-1}$heterocyclyl; and

-$S(O)_{0-2}$–$(alkyl)_{0-1}$(substituted heterocyclyl);

$R_2$ is selected from the group consisting of:

-hydrogen;

-alkyl;

-alkenyl;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-alkyl -O-alkyl;

-alkyl-O-alkenyl; and

-alkyl or alkenyl substituted by one or more substituents selected from the group consisting of:

-OH;

-halogen;

-$N(R_3)_2$;

-$CO\text{-}N(R_3)_2$;

-$CO\text{-}C_{1\text{-}10}$ alkyl;

-$CO\text{-}O\text{-}C_{1\text{-}10}$ alkyl;

-$N_3$;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-CO-aryl; and

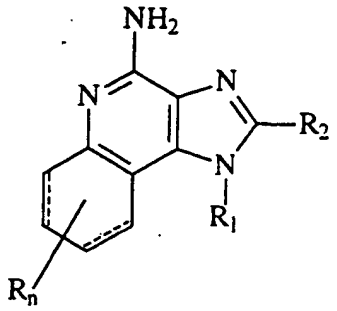
-CO-heteroaryl;

each $\mathbf{R_3}$ is independently selected from the group consisting of hydrogen; $C_{1\text{-}10}$ alkyl-heteroaryl; $C_{1\text{-}10}$ alkyl-(substituted heteroaryl); $C_{1\text{-}10}$ alkyl–aryl; $C_{1\text{-}10}$ alkyl–(substituted aryl) and $C_{1\text{-}10}$ alkyl;

**n** is 0 to 4;

and each **R** present is independently selected from the group consisting of $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halogen and trifluoromethyl, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

9. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula (Ib):



(Ib)

wherein

$R_1$ is -alkyl-$NR_3$-CO-$R_4$ or -alkenyl-$NR_3$-CO- $R_4$ wherein $R_4$ is heterocyclyl which may be unsubstituted or substituted by one or more substituents selected from the group consisting of:

-alkyl;

-alkenyl;

-alkynyl;

-$(alkyl)_{0-1}$-aryl;

-$(alkyl)_{0-1}$-(substituted aryl);

-$(alkyl)_{0-1}$-heterocyclyl;

-$(alkyl)_{0-1}$-(substituted heterocyclyl);

-$(alkyl)_{0-1}$-heteroaryl;

-$(alkyl)_{0-1}$-(substituted heteroaryl);

-O-alkyl;

-O-$(alkyl)_{0-1}$-aryl;

-O-$(alkyl)_{0-1}$-(substituted aryl);

-O-$(alkyl)_{0-1}$-heterocyclyl;

-O-$(alkyl)_{0-1}$-(substituted heterocyclyl);

-O-$(alkyl)_{0-1}$-heteroaryl;

-O-$(alkyl)_{0-1}$-(substituted heteroaryl);

-CO-aryl;

-CO-(substituted aryl);

-CO-heteroaryl;

-CO-(substituted heteroaryl);

-COOH;

-CO-O-alkyl;

-CO-alkyl;

-$S(O)_{0-2}$-alkyl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-aryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted aryl);

-$S(O)_{0-2}$-$(alkyl)_{0-1}$-heterocyclyl;

-$S(O)_{0-2}$-$(alkyl)_{0-1}$-(substituted heterocyclyl);

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-heteroaryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted heteroaryl);

-$P(O)(OR_3)_2$;

-$NR_3$-CO-O-alkyl;

-$N_3$;

oxo;

-halogen;

-$NO_2$;

-CN;

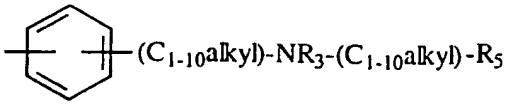
-haloalkyl;

-O-haloalkyl;

-CO-haloalkyl;

-OH; and

-SH; or $\mathbf{R_4}$ is




wherein $\mathbf{R_5}$ is an aryl, (substituted aryl), heteroaryl, (substituted heteroaryl), heterocyclyl or (substituted heterocyclyl) group;

$\mathbf{R_2}$ is selected from the group consisting of:

-hydrogen;

-alkyl;

-alkenyl;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-alkyl -O-alkyl;

-alkyl-O-alkenyl; and

-alkyl or alkenyl substituted by one or more substituents selected from the group consisting of:

-OH;

-halogen;

-$N(R_3)_2$;

-$CO\text{-}N(R_3)_2$;

-$CO\text{-}C_{1\text{-}10}$ alkyl;

-$CO\text{-}O\text{-}C_{1\text{-}10}$ alkyl;

-$N_3$;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-CO-aryl; and

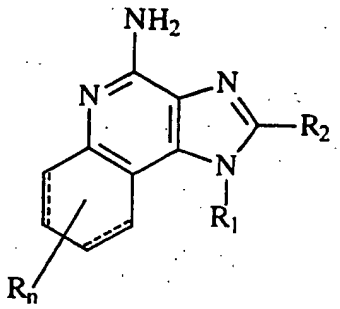
-CO-heteroaryl;

each $\mathbf{R_3}$ is independently selected from the group consisting of hydrogen; $C_{1\text{-}10}$ alkyl-heteroaryl; $C_{1\text{-}10}$ alkyl-(substituted heteroaryl); $C_{1\text{-}10}$ alkyl–aryl; $C_{1\text{-}10}$ alkyl–(substituted aryl) and $C_{1\text{-}10}$ alkyl;

**n** is 0 to 4;

and each **R** present is independently selected from the group consisting of $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halogen and trifluoromethyl, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

10. A compound of the formula (Ic):



(Ic)

wherein

$R_1$ is -alkyl-$NR_3$-CO-$R_4$ or -alkenyl-$NR_3$-CO- $R_4$ wherein $R_4$ is aryl, heteroaryl, heterocyclyl, alkyl or alkenyl, each of which may be unsubstituted or substituted by one or more substituents selected from the group consisting of:

-alkyl;

-alkenyl;

-alkynyl;

-$(alkyl)_{0-1}$-aryl;

-$(alkyl)_{0-1}$-(substituted aryl);

-$(alkyl)_{0-1}$-heteroaryl;

-$(alkyl)_{0-1}$-(substituted heteroaryl);

-$(alkyl)_{0-1}$-heterocyclyl;

-$(alkyl)_{0-1}$- (substituted heterocyclyl);

-O-alkyl;

-O-$(alkyl)_{0-1}$-aryl;

-O-$(alkyl)_{0-1}$-(substituted aryl);

-O-$(alkyl)_{0-1}$-heteroaryl;

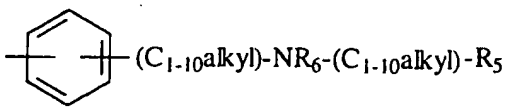
-O-$(alkyl)_{0-1}$-(substituted heteroaryl);

-O-$(alkyl)_{0-1}$-heterocyclyl;

-O-$(alkyl)_{0-1}$-(substituted heterocyclyl);

-CO-aryl;
-CO-(substituted aryl);
-CO-heteroaryl;
-CO-(substituted heteroaryl);
-COOH;
-CO-O-alkyl;
-CO-alkyl;
-$S(O)_{0-2}$-alkyl;
-$S(O)_{0-2}$–$(alkyl)_{0-1}$-aryl;
-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted aryl);
-$S(O)_{0-2}$–$(alkyl)_{0-1}$-heteroaryl;
-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted heteroaryl);
-$S(O)_{0-2}$–$(alkyl)_{0-1}$-heterocyclyl;
-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted heterocyclyl);
-$NR_6$-CO-O-alkyl;
-$P(O)(OR_3)_2$;
-$N_3$;
-halogen;
-$NO_2$;
-CN;
-haloalkyl;
-O-haloalkyl;
-CO-haloalkyl;
-OH;
-SH; and in the case of alkyl, alkenyl, or heterocyclyl, oxo;

or $\mathbf{R_4}$ is




wherein $\mathbf{R_5}$ is an aryl, (substituted aryl), heteroaryl, (substituted heteroaryl), heterocyclyl or (substituted heterocyclyl) group;

$\mathbf{R_2}$ is selected from the group consisting of:

-hydrogen;

-alkyl;

-alkenyl;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-alkyl -O-alkyl;

-alkyl-O-alkenyl; and

-alkyl or alkenyl substituted by one or more substituents selected from the group consisting of:

-OH;

-halogen;

-$N(R_6)_2$;

-CO-$N(R_6)_2$;

-CO-$C_{1-10}$ alkyl;

-CO-O-$C_{1-10}$ alkyl;

-$N_3$;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-CO-aryl; and

-CO-heteroaryl;

$R_3$ is selected from the group consisting of $C_{1-10}$ alkyl-heteroaryl; $C_{1-10}$ alkyl-(substituted heteroaryl); $C_{1-10}$ alkyl–aryl; $C_{1-10}$ alkyl–(substituted aryl) and $C_{1-10}$ alkyl;

each $R_6$ is independently selected from the group consisting of hydrogen; $C_{1-10}$ alkyl-heteroaryl; $C_{1-10}$ alkyl-(substituted heteroaryl); $C_{1-10}$ alkyl–aryl; $C_{1-10}$ alkyl–(substituted aryl) and $C_{1-10}$ alkyl;

n is 0 to 4;

and each R present is independently selected from the group consisting of $C_{1-10}$ alkyl, $C_{1-10}$ alkoxy, halogen and trifluoromethyl, or a pharmaceutically acceptable salt thereof.

11. A compound of claim 10 wherein the dashed bonds are absent.

12. A compound of claim 10 wherein $R_3$ is selected from the group consisting of $C_{1-10}$ alkyl-heteroaryl; $C_{1-10}$ alkyl-(substituted heteroaryl); $C_{1-10}$ alkyl–aryl; and $C_{1-10}$ alkyl–(substituted aryl).

13. A compound of claim 10 wherein $R_3$ is selected from the group consisting of $C_{1-10}$ alkyl-heteroaryl; $C_{1-10}$ alkyl-(substituted heteroaryl); $C_{1-10}$ alkyl–aryl; $C_{1-10}$ alkyl–(substituted aryl) and $C_{6-10}$ alkyl.

14. A compound of claim 10 wherein $R_3$ is selected from the group consisting of 2-methoxybenzyl; 2-furylmethyl; 3-furylmethyl; 2-nitrobenzyl; and 4-pyridylmethyl.

15. A compound of claim 14 wherein $R_2$ is hydrogen and $R_4$ is methyl.

16. A compound of claim 10 wherein n is 0.

17. A compound of claim 10 wherein $R_2$ is selected from the group consisting of hydrogen; alkyl; alkyl-O-alkyl; $(alkyl)_{0-1}$ aryl, $(alkyl)_{0-1}$-(substituted aryl); $(alkyl)_{0-1}$-heteroaryl; and $(alkyl)_{0-1}$-(substituted heteroaryl).

18. A compound of claim 10 wherein $R_2$ is selected from the group consisting of hydrogen; $C_{1-4}$ alkyl; and $C_{1-4}$alkyl-O-$C_{1-4}$alkyl.

19. A compound of claim 10 wherein $R_1$ is $-(CH_2)_{1-6}-NR_3-CO-R_4$-.

20. A compound of claim 10 wherein $R_4$ is naphthyl that may be unsubstituted or substituted by one or more substituents selected from the group consisting of:

-alkyl;
-alkenyl;
-alkynyl;
$-(alkyl)_{0-1}$-aryl;
$-(alkyl)_{0-1}$-(substituted aryl);
$-(alkyl)_{0-1}$-heteroaryl;
$-(alkyl)_{0-1}$-(substituted heteroaryl);
-O-alkyl,
$-O-(alkyl)_{0-1}$-aryl;
$-O-(alkyl)_{0-1}$-(substituted aryl);
$-O-(alkyl)_{0-1}$-heteroaryl;
$-O-(alkyl)_{0-1}$-(substituted heteroaryl);
-CO-aryl;
-CO-(substituted aryl);
-CO-heteroaryl;
-CO-(substituted heteroaryl);
-CO-O-alkyl;
-CO-alkyl;
-COOH;
$-S(O)_{0-2}$ -alkyl;
$-S(O)_{0-2}-(alkyl)_{0-1}$-aryl;
$-S(O)_{0-2}-(alkyl)_{0-1}$-(substituted aryl);
$-S(O)_{0-2}-(alkyl)_{0-1}$-heteroaryl;
$-S(O)_{0-2}-(alkyl)_{0-1}$-(substituted heteroaryl);
$-NR_3$-CO-O-alkyl;
$-P(O)(OR_3)_2$;
$-N_3$;
oxo;

-halogen;

$-NO_2$;

-CN;

-haloalkyl;

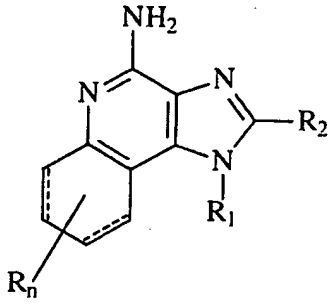
-O-haloalkyl;

-CO-haloalkyl;

-OH; and

-SH.

21. A compound of the formula (Id):



(Id)

wherein

$R_1$ is -alkyl-$NR_3$-CO-$R_4$ or -alkenyl-$NR_3$-CO- $R_4$ wherein $R_4$ is aryl or heteroaryl which may be unsubstituted or substituted by one or more substituents selected from the group consisting of:

-alkyl;

-alkenyl;

-alkynyl;

-$(alkyl)_{0-1}$-aryl;

-$(alkyl)_{0-1}$-(substituted aryl);

-$(alkyl)_{0-1}$-heteroaryl;

-$(alkyl)_{0-1}$-(substituted heteroaryl);

-$(alkyl)_{0-1}$-heterocyclyl;

-(alkyl)$_{0-1}$- (substituted heterocyclyl);

-O-alkyl;

-O-(alkyl)$_{0-1}$-aryl;

-O-(alkyl)$_{0-1}$-(substituted aryl);

-O-(alkyl)$_{0-1}$-heteroaryl;

-O-(alkyl)$_{0-1}$-(substituted heteroaryl);

-O-(alkyl)$_{0-1}$-heterocyclyl;

-O-(alkyl)$_{0-1}$-(substituted heterocyclyl);

-CO-aryl;

-CO-(substituted aryl);

-CO-heteroaryl;

-CO-(substituted heteroaryl);

-CO-O-alkyl;

-COOH;

-CO-alkyl;

-S(O)$_{0-2}$-alkyl;

-S(O)$_{0-2}$–(alkyl)$_{0-1}$-aryl;

-S(O)$_{0-2}$–(alkyl)$_{0-1}$-(substituted aryl);

-S(O)$_{0-2}$–(alkyl)$_{0-1}$-heteroaryl;

-S(O)$_{0-2}$–(alkyl)$_{0-1}$-(substituted heteroaryl);

-S(O)$_{0-2}$–(alkyl)$_{0-1}$-heterocyclyl;

-S(O)$_{0-2}$–(alkyl)$_{0-1}$-(substituted heterocyclyl);

-NR$_3$-CO-O-alkyl;

-P(O)(OR$_3$)$_2$;

-N$_3$;

-halogen;

-NO$_2$;

-CN;

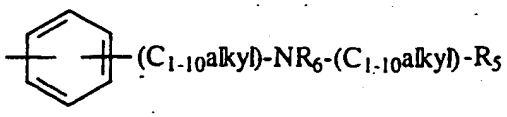
-haloalkyl;

-O-haloalkyl;

-CO-haloalkyl;

-OH; and

-SH; or $R_4$ is



wherein $R_5$ is an aryl, (substituted aryl), heteroaryl, (substituted heteroaryl), heterocyclyl or (substituted heterocyclyl) group;

$R_2$ is selected from the group consisting of:

-hydrogen;

-alkyl;

-alkenyl;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-alkyl -O-alkyl;

-alkyl-O-alkenyl; and

-alkyl or alkenyl substituted by one or more substituents selected from the group consisting of:

-OH;

-halogen;

-$N(R_3)_2$;

-$CO\text{-}N(R_3)_2$;

-$CO\text{-}C_{1\text{-}10}$ alkyl;

-$CO\text{-}O\text{-}C_{1\text{-}10}$ alkyl;

-$N_3$;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-CO-aryl; and

-CO-heteroaryl;

each $R_3$ is independently selected from the group consisting of hydrogen; $C_{1-10}$ alkyl-heteroaryl; $C_{1-10}$ alkyl-(substituted heteroaryl); $C_{1-10}$ alkyl–aryl; $C_{1-10}$ alkyl–(substituted aryl) and $C_{1-10}$ alkyl;

**n** is 0 to 4;

and each **R** present is independently selected from the group consisting of $C_{1-10}$ alkyl, $C_{1-10}$ alkoxy, halogen and trifluoromethyl, or a pharmaceutically acceptable salt thereof,

with the proviso that $R_4$ is not an unsubstituted benzene ring, and that when $R_4$ is a substituted benzene ring the substituents are selected from the group consisting of alkyl, alkoxy, alkylthio, hydroxy, haloalkyl, haloalkylcarbonyl, haloalkoxy, alkylcarbonyl, alkenylcarbonyl, arylcarbonyl, heteroarylcarbonyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, heterocycloalkyl, nitrile, alkoxycarbonyl, alkanoyloxy, alkanoylthio, and $-(C_{1-10}alkyl)-NR_3-(C_{1-10}alkyl)-R_5$, wherein $\mathbf{R_5}$ is an aryl, (substituted aryl), heteroaryl, (substituted heteroaryl), heterocyclyl or (substituted heterocyclyl) group.

22. A compound of claim 21 wherein n is 0.

23. A compound of claim 21 wherein $R_2$ is selected from the group consisting of hydrogen; alkyl; alkyl-O-alkyl; $(alkyl)_{0-1}aryl$; and $(alkyl)_{0-1}$ -(substituted aryl).

24. A compound of claim 21 wherein $R_2$ is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, and $C_{1-4}alkyl-O-C_{1-4}alkyl$.

25. A compound of claim 24 wherein $R_2$ is hydrogen or methoxyethyl.

26. A compound of claim 21 wherein $R_1$ is $-(CH_2)_{1-6}-NR_3-CO-R_4-$.

27. A compound of claim 21 wherein $R_3$ is hydrogen.

28. A compound of claim 21 wherein $R_4$ is naphthyl, quinolinyl, isoquinolinyl or pyridyl that may be unsubstituted or substituted by one or more substituents selected from the group consisting of:

-alkyl;

-alkenyl;

-alkynyl;

-$(alkyl)_{0-1}$-aryl;

-$(alkyl)_{0-1}$-(substituted aryl);

-$(alkyl)_{0-1}$-heteroaryl;

-$(alkyl)_{0-1}$-(substituted heteroaryl);

-O-alkyl;

-O-$(alkyl)_{0-1}$-aryl;

-O-$(alkyl)_{0-1}$-(substituted aryl);

-O-$(alkyl)_{0-1}$-heteroaryl;

-O-$(alkyl)_{0-1}$-(substituted heteroaryl);

-CO-aryl;

-CO-(substituted aryl);

-CO-heteroaryl;

-CO-(substituted heteroaryl);

-COOH;

-CO-O-alkyl;

-CO-alkyl;

-$S(O)_{0-2}$-alkyl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-aryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted aryl);

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-heteroaryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted heteroaryl);

-$NR_3$-CO-O-alkyl;

-$P(O)(OR_3)_2$;

-$N_3$;

-halogen;

-$NO_2$;

-CN;

-haloalkyl;

-O-haloalkyl;

-CO-haloalkyl;

-OH; and

-SH.

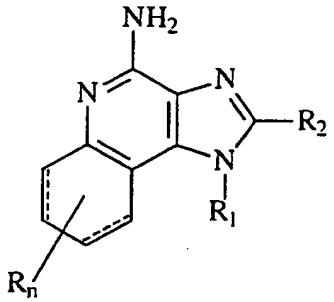
29. A compound of claim 28 wherein:

$R_2$ is selected from the group consisting of hydrogen; alkyl; alkyl-O-alkyl; $(alkyl)_{0-1}aryl$; and $(alkyl)_{0-1}$ -(substituted aryl);

$R_3$ is hydrogen; and

n is 0.

30. A compound of the formula (Ie):



(Ie)

wherein

$R_1$ is -alkyl-$NR_3$-CO-$R_4$ or -alkenyl-$NR_3$-CO- $R_4$ wherein $R_4$ is an alkyl or alkenyl group that is substituted by one or more substituents selected from the group consisting of:

-alkynyl;

-(substituted aryl) wherein the substituent(s) is selected from the group consisting of alkyl, alkoxy, alkylthio, hydroxy, haloalkyl, haloalkylcarbonyl, haloalkoxy, alkylcarbonyl, alkenylcarbonyl, arylcarbonyl, heteroarylcarbonyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, heterocycloalkyl, nitrile, alkoxycarbonyl, alkanoyloxy, and alkanoylthio;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-O-alkyl;

-O-$(alkyl)_{0-1}$-(substituted aryl) wherein the substituent(s) is selected from the group consisting of alkyl, alkoxy, alkylthio, hydroxy, haloalkyl, haloalkylcarbonyl, haloalkoxy, alkylcarbonyl, alkenylcarbonyl, arylcarbonyl, heteroarylcarbonyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, heterocycloalkyl, nitrile, alkoxycarbonyl, alkanoyloxy, and alkanoylthio;

-O-$(alkyl)_{0-1}$-heteroaryl;

-O-$(alkyl)_{0-1}$-(substituted heteroaryl);

-CO-aryl;

-CO-(substituted aryl);

-CO-heteroaryl;

-CO-(substituted heteroaryl);

-COOH;

-CO-O-alkyl;

-CO-alkyl;

-$S(O)_{0-2}$-alkyl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-aryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted aryl);

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-heteroaryl;

-$S(O)_{0-2}$–$(alkyl)_{0-1}$-(substituted heteroaryl);

-$NR_3$-CO-O-alkyl;

-$P(O)(OR_3)_2$;

-$N_3$;

oxo;

-$NO_2$;

-CN;

-O-haloalkyl;

-CO-haloalkyl;

-OH; and

-SH;

$R_2$ is selected from the group consisting of:

-hydrogen;

-alkyl;

-alkenyl;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-alkyl -O-alkyl;

-alkyl-O-alkenyl; and

-alkyl or alkenyl substituted by one or more substituents selected from the group consisting of:

-OH;

-halogen;

$-N(R_3)_2$;

$-CO-N(R_3)_2$;

$-CO-C_{1-10}$ alkyl;

$-N_3$;

-aryl;

-(substituted aryl);

-heteroaryl;

-(substituted heteroaryl);

-heterocyclyl;

-(substituted heterocyclyl);

-CO-aryl; and

-CO-heteroaryl;

each $R_3$ is independently selected from the group consisting of hydrogen; $C_{1-10}$ alkyl-heteroaryl; $C_{1-10}$ alkyl-(substituted heteroaryl); $C_{1-10}$ alkyl–aryl; $C_{1-10}$ alkyl–(substituted aryl) and $C_{1-10}$ alkyl;

n is 0 to 4;

and each **R** present is independently selected from the group consisting of $C_{1-10}$ alkyl, $C_{1-10}$ alkoxy, halogen and trifluoromethyl, or a pharmaceutically acceptable salt thereof.

31. A compound of claim 30 wherein n is 0.

32. A compound of claim 30 wherein $R_2$ is selected from the group consisting of hydrogen, alkyl, alkyl-O-alkyl, $(alkyl)_{0-1}$-aryl, and $(alkyl)_{0-1}$- (substituted aryl).

33. A compound of claim 30 wherein $R_2$ is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, and $C_{1-4}$alkyl-O-$C_{1-4}$alkyl.

34. A compound of claim 30 wherein $R_2$ is hydrogen or methoxyethyl.

35. A compound of claim 34 wherein n is 0.

36. A compound of claim 34 wherein $R_3$ is hydrogen and n is 0.

37. A compound of claim 30 wherein $R_3$ is hydrogen.

38. A pharmaceutical composition comprising a therapeutically effective amount of a compound selected from the group consisting of:

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]benzamide;
$N^1$-[4-(4-Amino-2-propyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]benzamide;
$N^1$-[4-(4-Amino-2-methyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]benzamide;
$N^1$-[4-(4-Amino-2-ethyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]benzamide;
$N^1$-[4-(4-Amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]benzamide;
$N^1$-[5-(4-Amino-2-methyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)pentyl]benzamide;
$N^1$-[5-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)pentyl]benzamide;
$N^1$-[3-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl]benzamide;

$N^1$-[2-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)ethyl]benzamide;

$N^1$-[3-(4-Amino-2-methyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl]benzamide;

$N^1$-[6-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)hexyl]benzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-3-phenylpropanamide;

$N^1$-[2-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)ethyl]-3-phenylpropanamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-phenoxyacetamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-ethylhexanamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-phenoxypropanamide ;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-2-chlorobenzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-3,4-dichlorobenzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-2,6-dichlorobenzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-4-fluorobenzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-4-chlorobenzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-4-methoxybenzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-4-(trifluoromethyl)benzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-2-phenylacetamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-(E)-3-phenyl-2-propenamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-3-cyclopentylpropanamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-1-cyclopentanecarboxamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-1-cyclohexanecarboxamide;

$N^1$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-1-yl]butyl}-2-methylbenzamide ;

$N^1$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-1-yl]butyl}-1-cyclopentanecarboxamide;

$N^1$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-1-yl]butyl}-1-cyclohexanecarboxamide,

$N^1$-{4-[4-Amino-2-(2-methoxyethyl)-6,7,8,9-tetrahydro-1*H*-imidazo[4,5-

c]quinolin-1-yl]butyl}benzamide;

$N^1$-{4-[4-Amino-2-(2-methoxyethyl)-6,7,8,9-tetrahydro-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-2-phenylacetamide;

$N^1$-[4-(4-Amino-2-(4-methoxybenzyl)-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]acetamide;

$N^1$-[4-(4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]acetamide;

$N^1$-[4-(4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-2,2,2-trifluoroacetamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-2,2,2-trifluoroacetamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-(*trans*)-2-phenylcyclopropane-1-carboxamide; and

$N^1$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-(*trans*)-2-phenylcyclopropane-1-carboxamide

in combination with a pharmaceutically acceptable carrier.

39. A compound selected from the group consisting of:

$N^6$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-6-quinolinccarboxamide;

$N^3$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-3-quinolinecarboxamide;

$N^3$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2,6-dimethoxynicotinamide;

$N^8$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-8-quinolinecarboxamide;

$N^3$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]nicotinamide;

$N^4$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]isonicotinamide;

$N^4$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-4-quinolinecarboxamide;

$N^4$-[4-(4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-phenyl-4-quinolinecarboxamide;

$N^3$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-(pentylsulfanyl)nicotinamide;

$N^3$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-6-cyanonicotinamide;

$N^3$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-6-chloronicotinamide;

$N^3$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-6-(2,2,2-trifluoroethoxy)nicotinamide;

$N^2$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-2-quinolinecarboxamide;

$N^1$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-1-isoquinolinecarboxamide;

$N^2$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-5-butyl-2-pyridinecarboxamide;

$N^3$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-3-indolecarboxamide;

$N^2$-{4-[4-Amino-2-(4-methoxybenzyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-2-quinolinecarboxamide;

$N^3$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-6-(1-pyrrolyl)nicotinamide;

$N^5$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-5-indolecarboxamide;

$N^3$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-5-(2-phenyl-1-ethynyl)nicotinamide;

$N^3$-[4-(4-Amino-2-phenyl-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]nicotinamide;

$N^2$-[4-(4-Amino-2-phenyl-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-quinolinecarboxamide;

$N^3$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-chloronicotinamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-(2-thienyl)acetamide;

$N^1$-[4-(4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-(3-thienyl)acetamide;

$N^2$-{4-[4-Amino-2-(4-methoxybenzyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-2-pyridinecarboxamide;

$N^3$-{4-[4-Amino-2-(4-methoxybenzyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-nicotinamide;

$N^4$-{4-[4-Amino-2-(2-methoxyethyl)-6,7,8,9-tetrahydro-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}isonicotinamide ;

$N^3$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-3-

furamide;

$N^3$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}nicotinamide;

$N^2$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-furamide;

$N^2$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-thiophenecarboxamide; and

$N^2$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-5-nitro-2-furamide.

40. A compound selected from the group consisting of:

$N^1$-[4-(4-Amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-5-(2-oxoperhydrothieno[3,4-*d*]imidazol-4-yl)pentanamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-5-(2-oxoperhydrothieno[3,4-*d*]imidazol-4-yl)pentanamide;

$N^1$-[2-(4-Amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)ethyl]-5-(2-iminoperhydrothieno[3,4-*d*]imidazol-4-yl)pentanamide;

$N^1$-[2-(4-Amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)ethyl]-5-(2-oxoperhydrothieno[3,4-*d*]imidazol-4-yl)pentanamide; and

$N^1$-[2-(4-Amino-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*]quinolin-1-yl)ethyl]-5-(2-oxoperhydrothieno[3,4-*d*]imidazol-4-yl)pentanamide.

41. A compounds selected from the group consisting of:

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-4-(morpholinomethyl)benzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-4-{[(4-pyridylmethyl)amino]methyl}benzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-4-{[(2-methoxyphenethyl)amino]methyl}benzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-4-({methyl[2-(2-pyridyl)ethyl]amino}methyl)benzamide;

$N^1$-{4-[4-Amino-2-(2-methoxycthyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-2-

oxo-2-phenylacetamide;

$N^1$-[4-(4-Amino -1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-4-[(2-tetrahydro-1*H* –1-pyrrolyl-1*H*-benzo[d]imidazol-1-yl)methyl]benzamide; and

$N^3$-[4-(4-Amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-6-morpholinonicotinamide.

42. A compound selected from the group consisting of:

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-ethoxy-1-naphthamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-4-cyanobenzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-3-cyanobenzamide;

$N^1$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-1-naphthamide;

$N^2$-[4-(4-Amino-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-naphthamide;

$N^1$-{4-[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl]butyl}-4-(1-pyrrolyl)benzamide;

$N^1$-{4-(4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl}-1-naphthamide;

$N^2$-{4-(4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl}-2-naphthamide;

$N^1$-{4-(4-Amino-2-(4-methoxybenzyl)-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl}-1-naphthamide;

$N^2$-{4-(4-Amino-2-(4-methoxybenzyl)-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl}-2-naphthamide;

$N^1$-[4-(4-Amino-2-butyl-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-1-naphthamide;

$N^2$-[4-(4-Amino-2-butyl-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-naphthamide;

$N^1$-[4-(4-Amino-6,7,8,9-tetrahydro-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-1-naphthamide; and

$N^2$-[4-(4-Amino-6,7,8,9-tetrahydro-1*H*-imidazo[4,5-c]quinolin-1-yl)butyl]-2-naphthamide.

43. A compound selected from the group consisting of:

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(4-methoxybenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(4-bromobenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(5-bromo-2-hydroxybenzyl)-acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(4-butoxybenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(2-chlorobenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(2-chloro-5-nitrobenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(5-chloro-2-nitrobenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-2-[(4-chlorophenyl)sulfanyl]benzylacetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(3,5-dichlorobenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(3,4-difluorobenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(2,5-dimethoxybenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(2,3-dimethoxybenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(2,4-dimethylbenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-[(5-ethyl-2-furyl)methyl]acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(2-furylmethyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(3-furylmethyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(3-phenylpropyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-octylacetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(1-naphthylmethyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-[(2-methoxy-1-naphthylmethyl]acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(4-nitrobenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(2-nitrobenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(4-pyridylmethyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(2-methylbenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(2,3,4-trimethoxybenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(3,4,5-trimethoxybenzyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-cyclopentylacetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-(4-fluorophenyl)acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-isopropylacetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-[4-(trifluoromethyl)phenyl]acetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-cyclohexylmethylacetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-benzylacetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-methylacetamide;

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-ethylacetamide; and

$N^1$-[4-(4-amino-1*H*-imidazo[4,5-*c*]quinolin-1-yl)butyl]-$N^1$-benzyl-2,2,2-trifluoroacetamide.

44. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 10 in combination with a pharmaceutically acceptable carrier.

45. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 21 in combination with a pharmaceutically acceptable carrier.

46. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 30 in combination with a pharmaceutically acceptable carrier.

47. A method of inducing cytokine biosynthesis in an animal comprising administering an effective amount of a composition of claim 1 to the animal.

48. A method of treating a viral disease in an animal comprising administering an effective amount of a composition of claim 1 to the animal.

49. A method of treating a neoplastic disease in an animal comprising administering an effective amount of a composition of claim 1 to the animal.

50. A method of inducing cytokine biosynthesis in an animal comprising administering an effective amount of a composition of claim 8 to the animal.

51. A method of treating a viral disease in an animal comprising administering an effective amount of a composition of claim 8 to the animal.

52. A method of treating a neoplastic disease in an animal comprising administering an effective amount of a composition of claim 8 to the animal.

53. A method of inducing cytokine biosynthesis in an animal comprising administering an effective amount of a composition of claim 9 to the animal.

54. A method of treating a viral disease in an animal comprising administering an effective amount of a composition of claim 9 to the animal.

55. A method of treating a neoplastic disease in an animal comprising administering an effective amount of a composition of claim 9 to the animal.

56. A method of inducing cytokine biosynthesis in an animal comprising administering an effective amount of a compound of claim 10 to the animal.

57. A method of treating a viral disease in an animal comprising administering an effective amount of a compound of claim 10 to the animal.

58. A method of treating a neoplastic disease in an animal comprising administering an effective amount of a compound of claim 10 to the animal.

59. A method of inducing cytokine biosynthesis in an animal comprising administering an effective amount of a compound of claim 21 to the animal.

60. A method of treating a viral disease in an animal comprising administering an effective amount of a compound of claim 21 to the animal.

61. A method of treating a neoplastic disease in an animal comprising administering an effective amount of a compound of claim 21 to the animal.

62. A method of inducing cytokine biosynthesis in an animal comprising administering an effective amount of a compound of claim 30 to the animal.

63. A method of treating a viral disease in an animal comprising administering an effective amount of a compound of claim 30 to the animal.

64. A method of treating a neoplastic disease in an animal comprising administering an effective amount of a compound of claim 30 to the animal.

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/15702

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) :A61K 31/437; A61P 31/12, 35/00; C07D 471/04
US CL :514/293; 546/82

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/293; 546/82

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | WO 98/30562 A1 (TERUMO KABUSHIKI KAISHA) 16 July 1998 (16.07.98), see entire document, especially page 88, Example 51 and page 90, Example 53. | 1-3, 5, 8, 10, 13, 16-27, 30-37, 44-49, 56-64 |
| X | JP 9-208584 A2 (TERUMO CORP.) 12 August 1997 (12.08.97), page 2, formula (I). | 8, 50, 51 |
| A | US 5,352,784 A (NIKOLAIDES et al.) 04 October 1994 (04.10.94), see entire document, especially columns 4-6. | 1-64 |

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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| * | Special categories of cited documents: | "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| "A" | document defining the general state of the art which is not considered to be of particular relevance | "X" | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
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| Date of the actual completion of the international search<br>24 AUGUST 2000 | Date of mailing of the international search report<br>22 SEP 2000 |
| Name and mailing address of the ISA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231<br>Facsimile No. (703) 305-3230 | Authorized officer<br>EVELYN HUANG<br>Telephone No. (703) 308-1235 |

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